FILE 'HOME' ENTERED AT 10:18:00 ON 03 MAY 2004)

	FILE 'MEDLINE, CANCERLIT, BIOTECHDS, EMBASE, CAPLUS' ENTERED AT 10:18:25
	ON 03 MAY 2004
L1	217588 S TUMOR SUPPRESSOR GENE OR P53 OR RB
L2	47380 S RETROVIR? AND (IN VITRO OR EX VIVO OR CULTURED OR CELL LIN?)
L3	1406 S L1 AND L2
L4	5155116 S LEUKEUMIA OR BLOOD OR BONE MARROW OR HEMATOPOIETIC
L5	150 S L4 AND L3
L6	3404355 S TUMOR OR CANCER OR METAST?
L7	110 S L6 AND L5
L8	1213838 S PURG? OR IMPLAN? OR TRANSPLA?
L9	38 S L8 AND L7
L10	20 DUP REM L9 (18 DUPLICATES REMOVED)

L10 ANSWER 19 OF 20 MEDLINE on STN DUPLICATE 8

AN 92083531 MEDLINE

DN PubMed ID: 1727382

TI Suppression of acute lymphoblastic leukemia by the human wild-type **p53** gene.

AU Cheng J; Yee J K; Yeargin J; Friedmann T; Haas M

CS UCSD Cancer Center, Department of Pathology, La Jolla 92093-0063.

SO Cancer research, (1992 Jan 1) 52 (1) 222-6. Journal code: 2984705R. ISSN: 0008-5472.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199201

ED Entered STN: 19920209

Last Updated on STN: 19970203 Entered Medline: 19920117

Independent mutations in both alleles of the p53 tumor AΒ suppressor gene are a frequent finding in human T-cell acute lymphoblastic leukemia (T-ALL) cell lines and in the cells of some T-ALL patients in relapse. One major goal of studying the status of p53 (and other tumor suppressor genes) in human cancer is to facilitate the suppression of the tumorigenic phenotype through the restoration of the expression of the wild-type allele. While the efficient insertion of a suppressor into all cells of solid/metastatic human tumors may at present be impossible, insertion into leukemia cells may be feasible due to the accessibility of the leukemia cells in the body. To examine the feasibility of suppressing the tumorigenicity of human T-leukemia cells, the human T-ALL cell line Be-13, which lacks endogenous p53 protein, was infected with a recombinant retrovirus encoding the wild-type allele of human p53 (hwtp53). Expression of p53 reduced the growth rate of infected Be-13 cells in vitro, suppressed colony formation in methylcellulose cultures, and abrogated their tumorigenic phenotype in nude mice in vivo. These results suggest that suppression of the leukemic phenotype of relapse T-ALL-derived Be-13 cells is feasible. Acute leukemia cell suppression via high-efficiency infection with retroviruses encoding wtp53 may be feasible and beneficial in T-ALL cases as part of a bone marrow transplantation regimen in an effort to reduce the frequency of

transplantation regimen in an effort to reduce the frequency of posttransplantation relapse.

L10 ANSWER 16 OF 20 MEDLINE on STN DUPLICATE 5

AN 1998133164 MEDLINE

DN PubMed ID: 9472561

TI Expression of exogenous wt-p53 does not affect normal hematopoiesis: implications for bone marrow purging.

AU Scardigli R; Bossi G; Blandino G; Crescenzi M; Soddu S; Sacchi A

CS Molecular Oncogenesis Laboratory, Regina Elena Cancer Institute, Rome, Italy.

SO Gene therapy, (1997 Dec) 4 (12) 1371-8. Journal code: 9421525. ISSN: 0969-7128.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199803

ED Entered STN: 19980312 Last Updated on STN: 19980312 Entered Medline: 19980303

Some gene therapy approaches for cancer treatment attempt to AΒ transduce onco-suppressor genes into tumor cells. A central problem of this strategy is the targeting of tumor cells to avoid damage to normal ones. It has been noticed that transduction of wtp53 into a large number of cancer cells induces tumor suppression. In contrast, some observations suggest that introduction of exogenous wt-p53 into nontransformed cells does not impair proliferation. If normal bone marrow (BM) cells are not affected by wt-p53 transduction, BM purging from p53-responding leukemic cells might be achieved in vitro by delivering the wild-type onco-suppressor to all marrow cells. We undertook a series of experiments to assess whether transduction of wt-p53 into normal hematopoietic cells is harmful. Two different wt-p53-recombinant retroviruses were used to infect primary, murine BM cells. Expression of exogenous wt-p53 in these cells did not affect in vitro colony formation, and did not induce any observable effects on morphology and differentiation. In contrast, the same viruses suppressed the tumor phenotype of v-src-transformed 32D cells. These results might open the way to gene therapy approaches to leukemias with the p53 gene without the need to target specifically and uniquely the tumor cells, sparing the normal ones.

- L10 ANSWER 1 OF 20 MEDLINE on STN
- AN 2004025526 MEDLINE
- DN PubMed ID: 14724570
- TI Wild-type **p53** gene transfer is not detrimental to normal cells in vivo: implications for tumor gene therapy.
- AU Bossi Gianluca; Mazzaro Giuseppina; Porrello Alessandro; Crescenzi Marco; Soddu Silvia; Sacchi Ada
- CS Department of Experimental Oncology, Molecular Oncogenesis Laboratory, Regina Elena Cancer Institute, Via delle Messi d'Oro 156, Rome 00158, Italy.
- SO Oncogene, (2004 Jan 15) 23 (2) 418-25. Journal code: 8711562. ISSN: 0950-9232.
- CY England: United Kingdom
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 200402
- ED Entered STN: 20040116 Last Updated on STN: 20040204 Entered Medline: 20040203
- The p53 oncosuppressor is strictly maintained in an inactive AB form under normal conditions, while it is post-translationally activated by a variety of stresses, enacting different protective biological functions. Since one critical issue in cancer gene therapy is tumor specificity, we asked whether the tight p53 regulation applies also to exogenously transferred p53. In principle, this type of regulation could allow p53 gene transfer in both normal and tumor cells to produce detrimental effects only in the latter ones. Here, we report that primary bone marrow cells infected with a p53 recombinant retrovirus and transplanted into irradiated mice reconstitute the hematopoietic system, with no detectable alterations in any of its compartments. Furthermore, simultaneous infection of leukemia and bone marrow cells depleted the neoplastic contamination, allowing lifelong, disease-free survival of 65% of the transplanted animals. These results show that exogenous p53 is controlled as tightly as the endogenous one, and opens the way to p53 gene therapy, without requiring tumor targeting.